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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/679,776	10/05/2000	Richard D. Granstein	2650/1F966-US1	8709

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Darby & Darby PC
805 Third Avenue
New York, NY 10022

EXAMINER	
LI, QIAN JANICE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 09/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	**Application No.** 09/679,776	**Applicant(s)** GRANSTEIN, RICHARD D.
	Examiner Q. Janice Li	**Art Unit** 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/23/04* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *32-36,43-46 and 51-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *35 and 36* is/are allowed.

6)☒ Claim(s) *32,33,43-46 and 51-53* is/are rejected.

7)☒ Claim(s) *34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 October 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment, and response submitted on 6/23/04 have been entered. Claims 37-42 and 47-49 have been cancelled; and claims 50-53 are newly submitted. Claims 32-36, 43-46, and 50-53 are pending, and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments would be addressed to the extent that they apply to current rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43-46 <u>stand</u> rejected and claims 50-53 are <u>newly</u> rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inducing tolerance to an allogenic transplant antigen in a subject by intravenously administering total cellular RNA or total cellular mRNA *prior to* the allogenic transplantation, wherein the cells are from the *graft tissue* or spleen cells, does not reasonably provide enablement for inducing tolerance to an allogenic transplant tissue by intravenous administering total cellular RNA/mRNA from any cells at any time. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In the 6/23/04 response, Applicants first argue that the antigen specificity is instantly provided by RNA, a person of ordinary skill in the art would be able to select appropriate cell types.

The argument has been fully considered but found not persuasive. This is because the claims are given the broadest reasonable interpretation, and as such, instant claims broadly encompass administering RNA from any cell and any source, not limited to cells that contain the antigen. This is contrary to the teaching of the specification, which states, "the RNA can be total cellular RNA from tissues containing the antigen, total cellular mRNA from tissues containing the antigen, or mRNA encoding the antigen" (Specification, page 6, lines 21-23); and the working example shows that intravenous injection of unrelated RNA would not induce tolerance (Specification, page 28, Results). It is noted that 35 U.S.C. § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970). Applicants are reminded that Claims must, under modern claim practice, stand alone to define invention, since, in patentability context, claims are to be given their broadest reasonable interpretations, and since limitations are not to be read into claims from specification. *In re Van Guens*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants then argue that the claims need not specify the timing of the RNA administration because it is not an inventive aspect of the present invention citing *In re Skrivan* as support.

The argument has been fully considered but found not persuasive. This is because in *In re Skrivan*, the disputed claims are written in Jepson style, and "THE DISPUTED LIMITATION DEALS ONLY WITH A PHYSICAL OPERATING CONDITION OF AN ADMITTEDLY OLD PROCESS", whereas the instant claims are not written in "Jepson" style, and the limitation does not deal with an admittedly old process. The limitation deals with the scope of an inventive process, and thus should be clearly set forth and commensurate with the enabled scope of the disclosure.

Accordingly, for reasons of record and those set forth above, the disclosure fails to meet the statutory enablement requirement.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 32 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Qiu et al* (Gene Ther 1996;3:262-68, IDS), taken with *Nair et al* (US 5,853,719, IDS).

Applicants argue that Qui does not teach total tumor RNA or that an immune response against a tumor can be created thereby, and there is no motivation to combine Qiu and Nair because Qiu and Nair use different routes of administration, and even if combined, there is no reasonable expectation of success.

The arguments have been fully considered but found not persuasive for reasons of record and following.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, *Qiu et al* is relied upon for a showing of intradermal administration of RNA, particularly mRNA, for the purpose of developing vaccine for cancer immunotherapy, whereas *Nair et al* supplemented the teaching of *Qiu et al* by establishing that it is well known in the art before the instant filing date that total cellular RNA is equally effective compared to mRNA, and could be used to circumvent the need of purifying RNA or isolating and identifying a tumor antigen in tumor immunotherapy. Although *Qiu et al* illustrated with mRNA encoding a model antigen (hAAT), not a tumor antigen, given the success in inducing immune response to the antigen in both *Qiu et al* and *Nair et al*, one of ordinary skilled would have had a reasonable expectation of success in eliciting an immune response against a tumor antigen. Moreover, both *Qiu et al and Nair et al* administer RNA into epidermal *dendritic cells,* the difference lies only whether the administration is directly *in vivo* or via *ex vivo*, and since both *Qiu et al and Nair et al* reported success in eliciting an immune response to the RNA encoded antigen, a reasonable success is expected when combine the teachings. Note that obviousness does not require absolute predictability of success; for obviousness under 35 U.S.C. § 103, all that is required is a reasonable expectation of success. See In re

O'Farrell, 7 USPQ2d 1673 (CAFC 1988). After all, the claim only requires an immune response against a tumor antigen is present.

Accordingly, for reasons of record and those set forth foregoing, the rejection stands.

Claim 33 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Qiu et al* (Gene Ther 1996;3:262-68, IDS), and *Nair et al* (US 5,853,719, IDS) as applied to claim 32 above, and further in view of *Segal et al* (US 6,403,080).

The applicant argues that Segal does not teach that an immune response to tumor can be induced by intradermally administering total tumor cell RNA.
In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In the instant case, "an immune response to tumor can be induced by intradermally administering total tumor cell RNA" was taught by the combined teachings of *Qiu et al* and *Nair et al*; *Segal et al* supplemented the teaching of *Qiu et al* and *Nair et al* by establishing that both B16 melanoma and fibrosarcoma cells could be used for developing tumor vaccine (column 29, example 2). It is the combined teachings that render the instant claims obvious.

Accordingly, the rejection stands.

Claim Objections

Claim 34 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Claims 35 and 36 are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

Any inquiry of formal matters can be directed to the patent analyst, **Dianiece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Q. Janice Li
Primary Examiner
Art Unit 1632

QJL
September 10, 2004